Institute of Experimental Morphology, Pathology and Anthropology with Museum
Bulgarian Anatomical Society

Acta morphologica et anthropologica, 19
Sofia • 2012

Serum IgG and IgM antibodies to GD1a ganglioside in adults – preliminary data

V. Kolyovska, D. Deleva

Institute of Experimental Morphology, Pathology and Anthropology with Museum, Bulgarian Academy of Sciences, Sofia

Over the past few years it is of critical importance to establish the clinical significance of serum IgG and IgM anti-GD1a antibodies as potential biomarkers of neuronal damage in immune-mediated neuropathies and neurodegenerative diseases. In this study the diagnostic value of IgG and IgM anti-GD1a antibodies was determined by ELIZA method in the serum of 11 adult patients (70-81 years). Significantly elevated serum antiganglioside IgG and IgM antibodies titers were detected only in three patients. These data suggest the immune-mediated neurodegeneration and antibody -mediated neuropathies. Therefore, IgG and IgM anti-GD1a antibodies can serve as hallmarkers lead to nervous system dysfunction.

Key words: serum IgG and IgM anti-GD1a antibodies

Introduction

Gangliosides are a family of acidic glycosphingolipids highly concentrated in the nervous system, where they represent about 10% of the total lipid content. The ganglioside spectra of normal blood plasma are remarkably stable, but show pronounced changes in pathological conditions [5]. GD1a is one of the major central nervous system neuronal ganglioside fraction. In our previous studies a considerable increase of serum GD1a ganglioside was determined in MS (neurodegenerative multifactorial disorder with an autoimmune component) [9,10,11]. Autoantobodies against gangliosides GM1 or GD1a are associated with acute motor axonal neuropathy and acute motor-sensory axonal neuropathy [7]. That'swhy, over the past few years it is of critical importance to establish the clinical significance of serum IgG and IgM anti-GD1a antibodies as potential biomarkers for the diagnosis, classification, disease activity and prediction of clinical courses in anti-ganglioside antibody-mediated neurodegenerative disorders.

No immunological studies about the possible role of serum IgG and IgM anti-GD1a antibodies in adults (over 70 years old) have been performed so far. Therefore, the aim of this study was to evaluate the levels of IgG and IgM anti-GD1a antibodies in the serum of these adult patients.

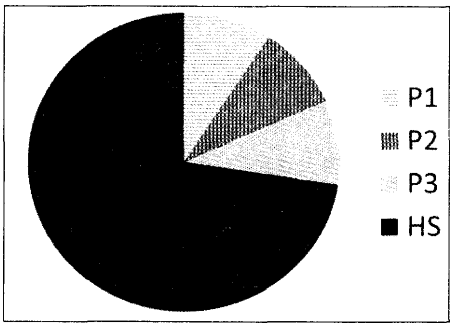

Fig.1. Percentage distribution of antiganglioside antibodies of the IgG and IgM class against GD1a ganglioside in adult patients
P1, P2, P3 – Adult patients; HS – Healthy subjects

Materials and Methods

Serum samples were obtained from 32 healthy subjects (middle age) and from 11 adult patients (70– 81 years) without neurological clinical symptoms. We determined antiganglioside antibodies (AGA) of the IgG and IgM class against GD1a ganglioside. The presence of anti-GD1a antibodies in the serum was measured by the enzyme-linked immunosorbent assay (ELISA). We made slight modifications of the method of Mitzutamari et al. [4,6]. As AGA were found in low titers in some healthy subjects we estimated a reference range for the healthy controls. Adult patients were considered strongly positive only if the optical density of their sera exceeded $x \pm 2$ SD of the healthy controls. The Student test was used to determine statistical differences between the groups using $p<0.05$ as the level of confidence.

Results and Discussion

The difference of optical density of serum IgG and IgM anti-GD1a antibodies between two groups (strongly positive adults and healthy subjects) was statistically significant. Elevated serum IgG and IgM titers to GD1a gangliosides were detected only in three adult patients (27.3 %) of the 11 studied adults. The remaining eight patients (72.7 %) had values similar to those of healthy controls (Fig. 1). Significantly elevated serum IgG and IgM antibodies titers to GD1a gangliosides in three adult patients in comparison with healthy subjects are shown in Fig. 2 and Fig. 3. Anti-ganglioside complex antibodies may be useful diagnostic and prognostic markers of the neuropathy [2]. Patients with a positive titer of anti-ganglioside antibodies had significant alterations of motor conduction parameters and contribute to the neuropathy [3]. In immune mediated neuropathies associated with antibodies to GM1, GD1a and GD1b the common mechanism is a complement mediated dysfunction and disruption of the nodes of Ranvier which causes a pathophysiological continuum from early reversible conduction failure to axonal degeneration [8]. These findings confirm a disease specific correlation between specific neuropathies and antiganglioside antibodies clinically useful [1].

In conclusion, our preliminary study permits us to find that: elevated titers of IgG and IgM anti– GD1a antibodies suggest the immune-mediated neurodegeneration; IgG and IgM anti–GD1a antibodies can serve as a biological marker for neuronal and

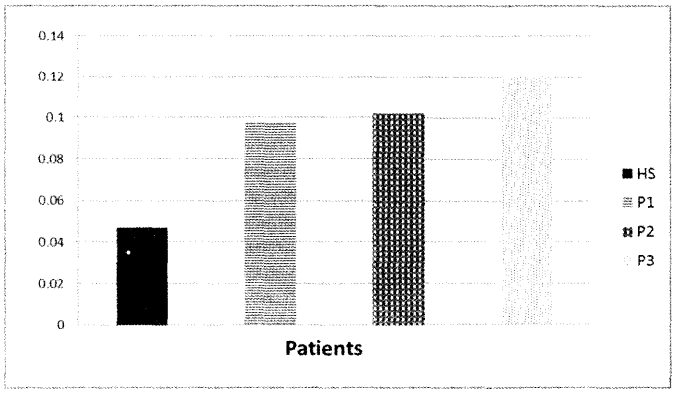

Fig.2. Serum IgG antibodies to GD1a in adults in comparison with healthy subjects

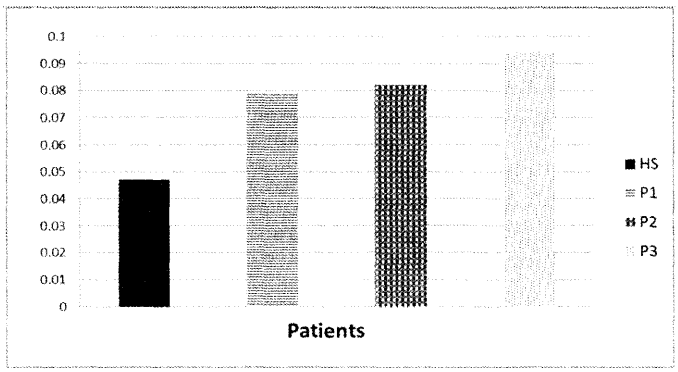

Fig.3. Serum IgM antibodies to GD1a in adults in comparison with healthy subjects

axonal damage, a very important indication for immediate neuroprotective treatment and its efficacy; there is not direct relationship between patient's age and the presence of symptomatic neurological damage.

References

1. Gallardo, E., R. Rojas-García, R. Belvís, C. Serrano-Munuera, E. Ortiz, N. Ortiz, J. Grau, I. Illa. Antiganglioside antibodies: when, which and for what. -Neurologia, 16 (7), 2001, 293-297.
2. Kusunoki, S. Immune-mediated neuropathies. – Rinsho Shinkeigaku., 49 (11), 2009, 956-958.
3. Matà, S., E. Betti, G. Masotti, F. Pinto, F. Lolli. Motor nerve damage is associated with anti-ganglioside antibodies in diabetes. – J Peripher Nerv Syst., 9 (3), 2004, 138-143.
4. Mizutamari, R.K., H. Wiegandt, G. Nores. Characterization of antiganglioside antibodies present in normal human plasma. – J. Neuroimmunol., 50 (2), 1994, 215-220.
5. Prokazova, N., L. Bergelson. Gangliosides and atherosclerosis. – Lipids, 29, 1994, 1-5.

6. Ravindranath, M.H., S. Muthugounder. Human antiganglioside autoantobodies: validation of ELISA. – Ann NY Acad Sci., 1050, 2005, 229 – 242.
7. Susuki, K., N. Yuki, D.P. Schafer, K. Hirata, G. Zhang, K. Funakoshi, M.N. Rasband. Dysfunction of nodes of Ranvier: a mechanism for anti-ganglioside antibody-mediated neuropathies. – Exp Neurol., 233 (1), 2012, 534-542.
8. Uncini, A. A common mechanism and a new categorization for anti-ganglioside antibody-mediated neuropathies. – Exp. Neurol., 235 (2), 2012, 513-516.
9. Zaprianova, E., D. Deleva, B. Sultanov, V. Kolyovska. Biological markers of neuronal damage and disturbed axon-oligodendroglial interactions in early multiple sclerosis. – Compt. Rend. Acad. Bulg. Sci., 61 (3), 2008, 407-412.
10. Zaprianova, E., D. Deleva, B. Sultanov, V. Kolyovska. Current knowledge of multiple sclerosis pathogenesis. – Acta morphol. et anthropol., 14, 2009, 136-140.
11. Zaprianova, E., S.S. Sergeeva, O.S. Sotnikov, D. Deleva, B. Sultanov, V. Kolyovska, T.V. Krasnova. Evidence of early neuronal damage in the serum of multiple sclerosis patients. – Compt. Rend. Acad. Bulg. Sci., 63 (3), 2010, 447-454.